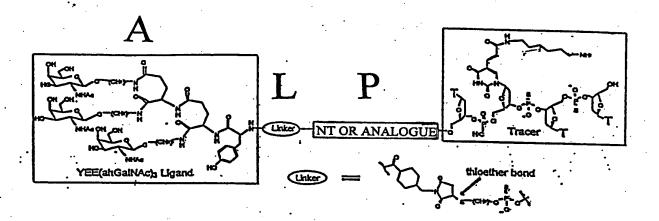
CROSS-LINKING REAGENT



Tri-antennary

X = NH, O, S Y = P or S Z = NH-alkyl, NH_2 , O, S A = NH, CH_2 , O, S n = 2 to 17 2-carbon units Carbohydrate = O

tris((heteroatom)methyl)-[heteroatom]methane

diglutamyI'

diasparatyl

FIGURE 3 (CONTINUED)

$$A \longleftrightarrow_{n} A \circlearrowleft_{n} A \hookrightarrow_{n} A \hookrightarrow_$$

tris((heteroatom)methyl)-[heteroatom]methane examples
tris(hydroxymethyl)aminomethane-based
[A= O]
tris(aminomethyl)aminomethane-based
[A= NH]
tris(thiomethyl)aminomethane-based
[A= S]

tris(aminomethyl)-[heteroatom]methane

tris(acetoxy)-[heteroatom]methane

Tetra-antennary

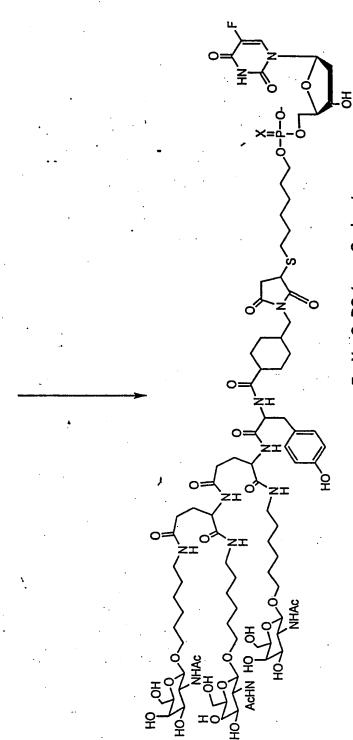
FIGURE 3 (CONTINUED)

oligopeptide-based (i.e. triglutamyl)

Multi-antennary

substituted polystyrene-based

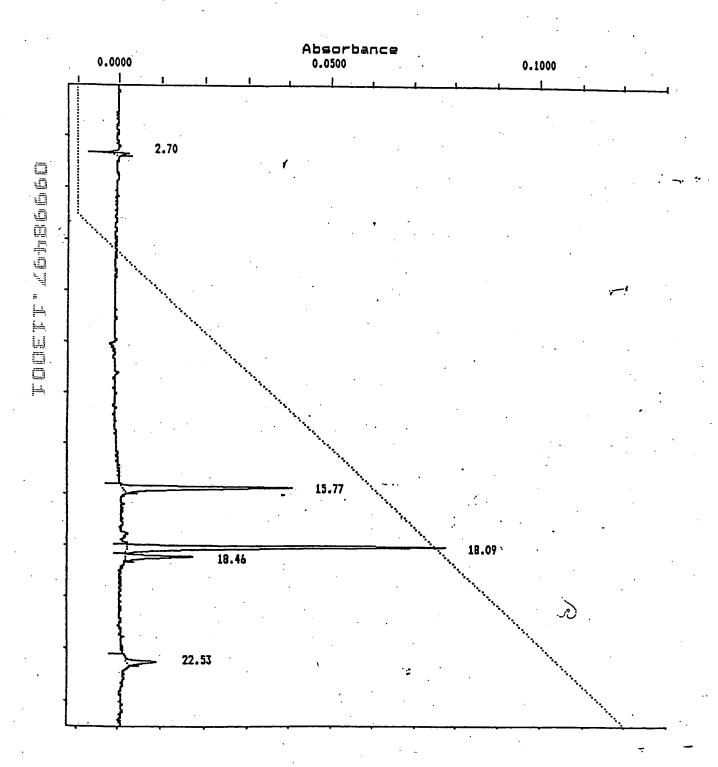
substituted poly(ethyleneglycol)

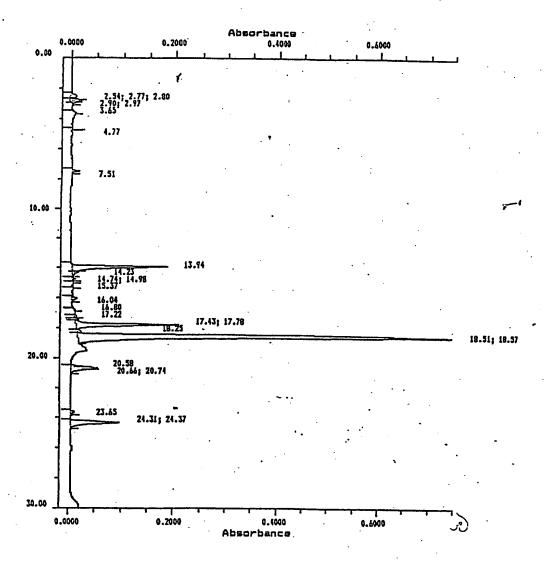


6a X=0 OH 6b X=S

7a X = 0; PO 1-mer Conjugate 7b X = S; PS 1-mer Conjugate

FIGURE 7





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(Lorr

R =-S-(CH₂)₈-OH

R= H

YEE(ah-GalNAc)1]-NH

Na_XPO₄, pH 7.0 # #

- 1) H+
- 2) 1H-tetrazole

3) Oxidation - Beaucage Reagent

4) Capping - Acetic anhydride, 2,6-Lutidine Tetrahydrofuran

5) Repeat

- 1) H+
- 2) 1H-tetrazole

- 3) Oxidation Beaucage Reagent
- 4) Capping Acetic anhydride, 2,6-Lutidine Tetrahydrofuran
- 5) H+
- 6) 0.1 M NaOH in 50% CH₃OH/H₂O, 1h, 25°C
- 7) C₁₈ ScpPak (Waters Corp.)